What is claimed is:

1. An automated method of reading a microarray comprising,

a) providing an initial representation of a microarray comprising a plurality of target spots illuminated by illumination light having a designated intensity;

b) determining from the initial representation whether at least one of the target spots has an emanating light intensity that is not between selected upper and lower threshold values, and designating such target spot a non-acceptable target spot; and,

c) modulating the designated intensity of the illumination light via an automated upstream selective light modulator located in an illumination light path substantially at a conjugate image plane of the sample to provide a modulated illumination light and an adjusted target spot that emanates an adjusted light intensity between the selected upper and lower threshold values.

2. The method of claim 1 wherein the method further comprises measuring the amount of modulation of the designated intensity of the illumination light and measuring the adjusted light intensity, then correlating the amount of modulation with the adjusted light intensity to provide a measure of the actual signal strength of the target spot.

3. The method of claim 2 wherein the method further comprises determining an amount of a probe located at the adjusted target spot from the measure of the actual signal strength of the target spot.

4. The method of claim 2 wherein the method is implemented according to a formula:

$$SS(x,y) = K * CCDS(x,y) / II(x,y)$$

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

5. The method of claim 2 wherein the method further comprises detecting a fluorescent target spot.

6. The method of claim 5 wherein the method is implemented according to a formula:

SS(x,y) = K *PB(II(x,y),fluoro)*CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro) is a photobleaching function based on illumination energy/intensity and a fluorophore being excited,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

7. The method of claim 5 wherein the method is implemented according to a formula:

SS(x,y) = K *PB(II(x,y),fluoro,x,y)*CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro,x,y) is a photobleaching function based on illumination energy/intensity, a fluorophore being excited, and a spatial variation term,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

8. The method of claim 2 wherein the modulated illumination light is modulated by changing its illumination intensity.

9. The method of claim 2 wherein the modulated illumination light is modulated by changing its duration of illuminating the target spot.

10. The method of claim 2 wherein the initial representation comprises a precompiled map of expected data for the target spots of the microarray.

11. The method of claim 2 wherein the initial representation comprises an initial image of the plurality of target spots illuminated by the illumination light having the designated intensity and taken by a same microarray reader that implements the determining, modulating, measuring and correlating.

12. The method of claim 11 wherein the initial image is taken substantially immediately before the determining, modulating, measuring and correlating are implemented.

13. The method of claim 2 wherein the method further comprises repeating the determining, modulating, measuring and correlating using the measure of the actual signal strength as the initial representation.

14. The method of claim 2 wherein the method further comprises selecting a probe such that the modulation is linearly related to the adjusted light intensity.

15. The method of claim 2 wherein the method is implemented using a microarray reader comprising the upstream selective light modulator, and a light detector disposed downstream from the microarray in a detection light path substantially at a conjugate image plane of the sample, wherein the selective light modulator and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the upstream selective light modulator and that compiles the modulated illumination light and the adjusted light intensity, and wherein the controller spatially varies the transmissive characteristics of the selective light modulator to vary the modulated illumination light impinging on the non-acceptable target spots of the microarray such that light emanating from the non-acceptable target spots is between the threshold levels.

16. The method of claim 15 wherein the upstream selective light modulator comprises a digital micromirror device.

17. The method of claim 15 wherein the detector comprises a charge coupled device.

18. An automated method of reading a microarray comprising,

a) providing an initial representation of a microarray comprising a plurality of target spots illuminated by illumination light having a designated intensity;

b) determining from the initial representation whether at least one of the target spots has an emanating light intensity that is not between selected upper and lower threshold values, and designating at least one of such target spots a non-acceptable target spot; and,

c) modulating the emanating light intensity via an automated downstream selective light modulator located in a detection light path

substantially at a conjugate image plane of the sample to provide a modulated detection light comprising an adjusted emanating light intensity that is between the selected upper and lower threshold values.

19. The method of claim 18 wherein the method further comprises measuring the amount of modulation of the detection light and measuring the modulated detection light, then correlating the amount of modulation with the modulated detection light to provide a measure of the actual signal strength of the target spot.

20. The method of claim 19 wherein the method further comprises determining an amount of a probe located at the non-acceptable target spot from the measure of the actual signal strength of the target spot.

21. The method of claim 19 wherein the method is implemented according to a formula:

$SS(x,y) = K * CCDS(x,y) / II(x,y)$

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

22. The method of claim 19 wherein the method further comprises detecting a fluorescent target spot.

23. The method of claim 22 wherein is implemented according to a formula:

$SS(x,y) = K * PB(II(x,y),fluoro) * CCDS(x,y) / II(x,y)$

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro) is a photobleaching function based on illumination energy/intensity and a fluorophore being excited,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

24. The method of claim 22 wherein the method is implemented according to a formula:

SS(x,y) = K *PB(II(x,y),fluoro,x,y)*CCDS(x,y) / II(x,y)
where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro,x,y) is a photobleaching function based on illumination energy/intensity, a fluorophore being excited, and a spatial variation term,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

25. The method of claim 19 wherein the initial representation comprises a precompiled map of expected data for the target spots of the microarray.

26. The method of claim 19 wherein the initial representation comprises an initial image of the plurality of target spots illuminated by the illumination light having the designated intensity and taken by a same microarray reader that implements the determining, modulating, measuring and correlating.

27. The method of claim 26 wherein the initial image is taken substantially immediately before the determining, modulating, measuring and correlating are implemented.

28. The method of claim 19 wherein the method further comprises repeating the determining, modulating, measuring and correlating using the measure of the actual signal strength as the initial representation.

29. The method of claim 19 wherein the method further comprises selecting a probe such that the modulation is linearly related to the adjusted light intensity.

30. The method of claim 19 wherein the method is implemented using a microarray reader comprising the selective light modulator, and a light detector disposed in a detection light path substantially at a conjugate image plane of the sample and downstream from the microarray and the downstream selective light modulator, wherein the selective light modulator and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the downstream selective light modulator and that compiles the modulated detection light and the adjusted light intensity, and wherein the controller selectively varies the transmissive characteristics of the selective light modulator to vary the modulated detection light impinging on the non-acceptable target spots of the microarray such that light received at the detector is between the threshold levels.

31. The method of claim 30 wherein the downstream selective light modulator comprises a digital micromirror device.

32. The method of claim 30 wherein the detector comprises a charge coupled device.

33. A microarray reader comprising an automated upstream selective light modulator located upstream of a microarray in an illumination light path substantially at a conjugate image plane of the sample, and a light detector disposed downstream from the microarray in a detection light path substantially at a conjugate image plane of the sample, wherein the selective light modulator and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the upstream selective light modulator and that compiles an amount of modulated illumination light when the upstream selective light modulator is modulated and an adjusted light intensity emanating from a target spot on a microarray receiving the modulated illumination light, and wherein the controller selectively varies the transmissive characteristics of the selective light modulator to vary the modulated illumination light impinging on at least one non-acceptable target spot of the microarray such that light emanating from the at least one non-acceptable target spot is between selected threshold levels.

34. The microarray reader of claim 33 wherein the controller further comprises computer-implemented programming that controls measuring the amount of modulation of the illumination light and controls measuring the adjusted light intensity, then correlates the amount of modulation with the adjusted light intensity to provide a measure of the actual signal strength of the target spot.

35. The microarray reader of claim 34 wherein the controller further comprises computer-implemented programming that determines an amount of

a probe located at the at least one non-acceptable target spot from the measure of the actual signal strength of the target spot.

36. The microarray reader of claim 34 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

37. The microarray reader of claim 34 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *PB(II(x,y),fluoro)*CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro) is a photobleaching function based on illumination energy/intensity and a fluorophore being excited,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

38. The microarray reader of claim 34 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *PB(II(x,y),fluoro,x,y)*CCDS(x,y) / II(x,y)
where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro,x,y) is a photobleaching function based on illumination energy/intensity, a fluorophore being excited, and a spatial variation term,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

39. The microarray reader of claim 34 wherein the controller further comprises computer-implemented programming comprising a precompiled map of expected data for the target spots of the microarray.

40. The microarray reader of claim 34 wherein the upstream selective light modulator comprises a digital micromirror device.

41. The microarray reader of claim 34 wherein the detector comprises a charge coupled device.

42. A microarray reader comprising an automated downstream selective light modulator located downstream of a microarray in a detection light path substantially at a conjugate image plane of the sample, and a light detector disposed in the detection light path substantially at a conjugate image plane of the sample and downstream from the downstream selective light modulator and the microarray, wherein the downstream selective light modulator and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the downstream selective light modulator and that compiles an amount of modulated detection light when the downstream selective light modulator is modulated and an adjusted light intensity received by the detector, and wherein the controller selectively varies the transmissive characteristics of the downstream selective light modulator to vary the modulated detection light emanating from at least one non-acceptable target

spot of the microarray such that light received at the detector from the at least one non-acceptable target spot is between selected threshold levels.

43. The microarray reader of claim 42 wherein the controller further comprises computer-implemented programming that controls measuring the amount of modulation of the detection light and controls measuring the adjusted light intensity, then correlates the amount of modulation with the adjusted light intensity to provide a measure of the actual signal strength of the target spot.

44. The microarray reader of claim 43 wherein the controller further comprises computer-implemented programming that determines an amount of a probe located at the at least one non-acceptable target spot from the measure of the actual signal strength of the target spot.

45. The microarray reader of claim 43 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

46. The microarray reader of claim 43 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *PB(II(x,y),fluoro)*CCDS(x,y) / II(x,y)

where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro) is a photobleaching function based on illumination energy/intensity and a fluorophore being excited,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

47. The microarray reader of claim 43 wherein the controller further comprises computer-implemented programming comprising the formula:

SS(x,y) = K *PB(II(x,y),fluoro,x,y)*CCDS(x,y) / II(x,y)
where,

SS(x,y) is the actual signal strength of the target spot,

K is a constant for the system,

PB(II(x,y),fluoro,x,y) is a photobleaching function based on illumination energy/intensity, a fluorophore being excited, and a spatial variation term,

(CCDS(x,y)) is the adjusted light intensity, and

(II(x,y)) is the modulated illumination light.

48. The microarray reader of claim 43 wherein the controller further comprises computer-implemented programming comprising a precompiled map of expected data for the target spots of the microarray.

49. The microarray reader of claim 43 wherein the downstream selective light modulator comprises a digital micromirror device.

50. The microarray reader of claim 43 wherein the detector comprises a charge coupled device.

51. An automated method of reading a microarray comprising,

a) providing an initial representation of a microarray comprising a plurality of target spots illuminated by illumination light having a designated intensity;

b) determining from the initial representation whether at least one of the target spots has an emanating light intensity that is not between selected upper and lower threshold values, and designating at least one of such target spots as a non-acceptable target spot;

c) selectively illuminating the non-acceptable target spot via selectively transmitting light to the microarray using a first automated upstream selective light modulator located in an illumination light path substantially at a conjugate image plane of the sample; and,

d) modulating the designated intensity of the illumination light via a second automated upstream selective light modulator located in the illumination light path substantially at a conjugate image plane of an aperture diaphragm of the objective lens, to provide a modulated illumination light and an adjusted target spot that emanates an adjusted light intensity between the selected upper and lower threshold values.

52. The method of claim 51 wherein the method further comprises measuring the amount of modulation of the designated intensity of the illumination light and measuring the adjusted light intensity, then correlating the amount of modulation with the adjusted light intensity to provide a measure of the actual signal strength of the target spot.

53. The method of claim 52 wherein the method further comprises also modulating the designated intensity of the illumination light via the first automated upstream selective light modulator located in the illumination light path substantially at the conjugate image plane of the sample.

54. The method of claim 52 wherein the method further comprises determining an amount of a probe located at the adjusted target spot from the measure of the actual signal strength of the target spot.

55. An automated method of reading a microarray comprising,

a) providing an initial representation of a microarray comprising a plurality of target spots illuminated by illumination light having a designated intensity;

b) determining from the initial representation whether at least one of the target spots has an emanating light intensity that is not between selected upper and lower threshold values, and designating at least one of such target spots as a non-acceptable target spot;

c) selectively detecting light from the non-acceptable target spot via selectively transmitting light from the microarray using a first automated downstream selective light modulator located in a detection light path substantially at a conjugate image plane of the sample; and,

d) modulating the emanating light intensity via a second automated downstream selective light modulator located in a detection light path substantially at a conjugate image plane of an aperture diaphragm of the objective lens, to provide a modulated detection light comprising an adjusted emanating light intensity between the selected upper and lower threshold values.

56. The method of claim 55 wherein the method further comprises measuring the amount of modulation of the emanating light intensity and measuring the modulated detection light, then correlating the amount of modulation with the modulated detection light to provide a measure of the actual signal strength of the target spot.

57. The method of claim 56 wherein the method further comprises also modulating the emanating light intensity of the detection light via the first automated downstream selective light modulator located in the detection light path substantially at the conjugate image plane of the sample.

58. The method of claim 56 wherein the method further comprises determining an amount of a probe located at the adjusted target spot from the measure of the actual signal strength of the target spot.

59. A microarray reader comprising a first automated upstream selective light modulator located upstream of a microarray in an illumination light path substantially at a conjugate image plane of the sample, a second automated upstream selective light modulator located upstream of the microarray in the illumination light path substantially at a conjugate image plane of an aperture diaphragm of the objective lens, and a light detector disposed downstream from the microarray in a detection light path substantially at a conjugate image plane of the sample, wherein the first and second selective light modulators and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the first and second upstream selective light modulators and that compiles an amount of modulated illumination light when the second upstream selective light modulator is modulated and an adjusted light intensity emanating from a target spot on a microarray receiving the modulated illumination light, and wherein the controller selectively varies the transmissive characteristics of the second selective light modulator to vary the modulated illumination light impinging on at least one non-acceptable target spot of the microarray such that light emanating from the at least one non-acceptable target spot is between selected threshold levels.

60. The microarray reader of claim 59 wherein the controller further comprises computer-implemented programming that controls measuring the amount of modulation of the illumination light and controls measuring the adjusted light intensity, then correlates the amount of modulation with the

adjusted light intensity to provide a measure of the actual signal strength of the target spot.

61. The microarray reader of claim 60 wherein the controller further comprises computer-implemented programming that determines an amount of a probe located at the at least one non-acceptable target spot from the measure of the actual signal strength of the target spot.

62. A microarray reader comprising a first automated downstream selective light modulator located downstream of a microarray in a detection light path substantially at a conjugate image plane of the sample, a second automated downstream selective light modulator located downstream of the microarray in the illumination light path substantially at a conjugate image plane of an aperture diaphragm of the objective lens, and a light detector disposed in the detection light path substantially at a conjugate image plane of the sample and downstream from the first and second downstream selective light modulators and the microarray, wherein the first and second selective light modulators and the light detector are operably connected to at least one controller containing computer-implemented programming that controls transmissive characteristics of the first and second downstream selective light modulator and that compiles an amount of modulated detection light when the second downstream selective light modulator is modulated and an adjusted emanating light intensity received by the detector, and wherein the controller selectively varies the transmissive characteristics of the second downstream selective light modulator to vary the modulated detection light emanating from at least one non-acceptable target spot of the microarray such that light received at the detector from the at least one non-acceptable target spot is between selected threshold levels.

63. The microarray reader of claim 62 wherein the controller further comprises computer-implemented programming that controls measuring the amount of modulation of the detection light and controls measuring the adjusted emanating light intensity, then correlates the amount of modulation with the adjusted emanating light intensity to provide a measure of the actual signal strength of the target spot.

64. The microarray reader of claim 63 wherein the controller further comprises computer-implemented programming that determines an amount of a probe located at the at least one non-acceptable target spot from the measure of the actual signal strength of the target spot.